

corpse is during the first 24 hours after death. By day 5, the amount of infectious virus has decreased by 96.48%. If proper biosafety precautions and personal protective equipment are used to handle the corpse during autopsy or preparation for burial or cremation, we believe that the burial or cremation process is unlikely to spread disease.

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## Guillain-Barré Syndrome Associated with COVID-19 Vaccination

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We conducted a multi-institutional study in Taiwan and a systematic review of the literature for reports of Guillain-Barré syndrome after coronavirus disease vaccination. This condition, mostly the classic form and the acute inflammatory demyelinating polyneuropathy subtype, has been reported in 39 cases and has occurred within 2 weeks of vaccine administration.

Guillain-Barré syndrome (GBS), an immune-mediated polyradiculoneuropathy with a ≈5% mortality rate, has an incidence worldwide of 0.81–1.91 cases/100,000 person-years (1). GBS has been

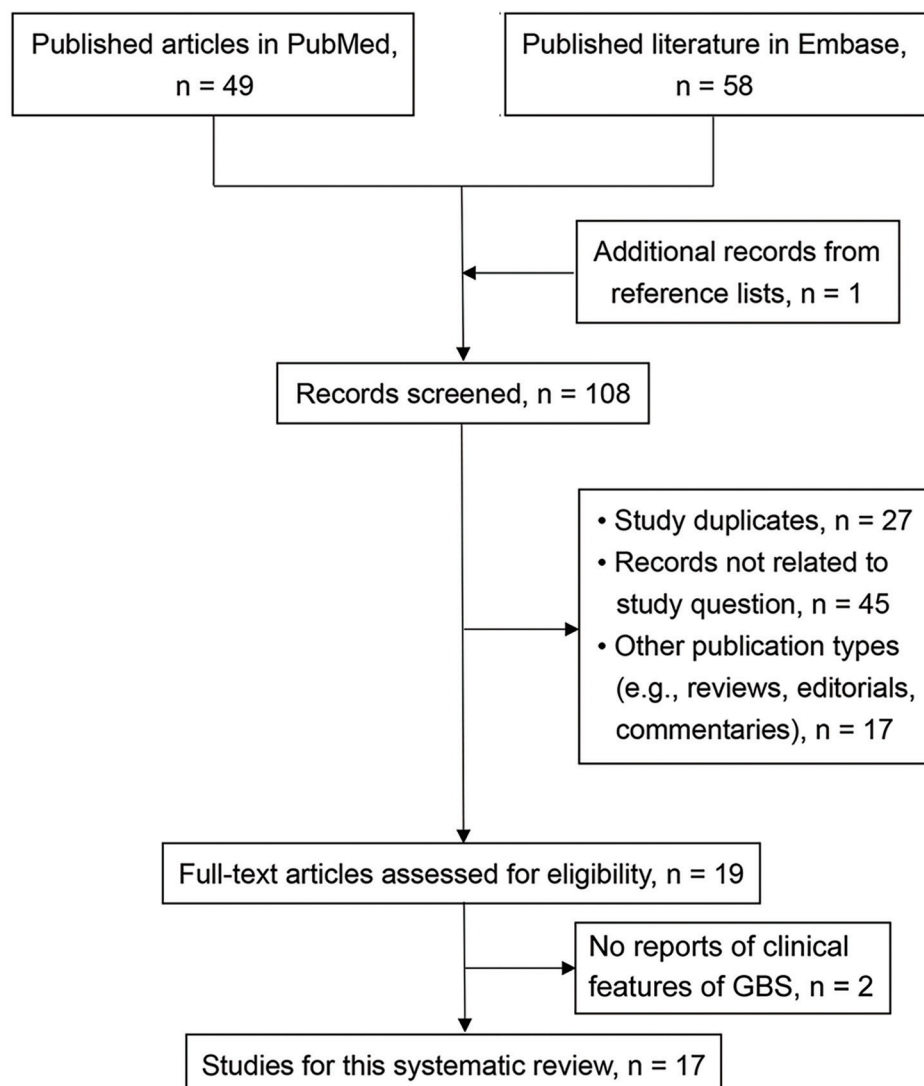
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reported to be associated with coronavirus disease (COVID-19) vaccination, but a comprehensive summary regarding this rare adverse event is still lacking. To determine clinical features of GBS associated with COVID-19 vaccination, we conducted hospital-based investigations in Taiwan along with a systematic review of published case reports.

We analyzed electronic medical records data from Taiwan's largest multi-institutional healthcare system, including 9 branches of Chang Gung Memorial Hospital (2), where healthcare workers received first-priority COVID-19 ChAdOx1-S vaccine (Oxford/AstraZeneca, <https://www.astrazeneca.com>) starting March 22, 2021. We included healthcare workers vaccinated during March 22–May 31 and followed them for 30 days after vaccination. We identified GBS cases on the basis of code G610 from the International Classification of Disease, 10th Revision,

Clinical Modification, or spontaneous adverse drug reaction reporting systems within the hospitals. Two authors (C.H.W. and S.C.L.) confirmed diagnosis and classification of GBS cases through chart reviews (3,4). This study was approved by the Institutional Review Board of Chang Gung Medical Foundation (approval no. 202101087B0).

To summarize clinical features of published cases from literature, we searched PubMed and Embase for reports posted through August 17, 2021, using relevant key terms such as "COVID-19," "Guillain-Barré syndrome," and "vaccine" with suitable MeSH terms. Two independent reviewers (S.C.S., C.H.W.) performed the study selection and data extraction; a third-reviewer (S.C.L.) settled any differences between them. We excluded cases with coexisting COVID-19 or preexisting GBS. We included only publications with reports of clinical features related



**Figure.** Systematic review of published literature in study of Guillain-Barré syndrome associated with coronavirus vaccination, 2021. GBS, Guillain-Barré syndrome.

to GBS. We described basic characteristics, laboratory data, pathologic reports, treatment patterns, and prognosis of GBS cases associated with COVID-19 vaccination. The study protocol of this systematic review is published on PROSPERO ([https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=265479](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=265479)).

We included 18,269 healthcare workers (mean age 40.6 years, range 18–87 years; 67.5% were women) who received ChAdOx1-S vaccine during the study period. After these 18,257 first-dose and 544 second-dose vaccinations, we identified 1 GBS case after a first dose of ChAdOx1-S vaccine in 1 of the hospitals participating in the study.

After a systematic review of published literature (Figure), we included 17 publications reporting an additional 38 cases of GBS related to COVID-19 vaccination (India, 10 cases; United Kingdom, 11 cases; Mexico, 7 cases; United States, 3 cases; France, 1 case; Italy, 3 cases; Malta, 1 case; Turkey, 1 case; and Qatar, 1 case) (Appendix Table, <https://wwwnc.cdc.gov/EID/article/27/12/21-1634-App1.pdf>). Including the case in Taiwan, these 39 cases occurred in persons with a mean age of 57.8 (range 20–86) years; 56.4% were male. Most of the reported case-patients received ChAdOx1-S (25/39), followed by BNT162b2 (12/39) (Pfizer-BioNTech, <https://www.pfizer.com>), Ad26.COV2.S (1/39) (Johnson & Johnson, <https://www.jnj.com>), and CoronaVac (1/39) (Sinovac Biotech, <http://www.sinovac.com>). The GBS rate after COVID-19 vaccination ranged from 1.8 to 53.2 cases/1 million doses. The initial symptoms of GBS included myalgia (12/39), paraparesis (5/39), quadriparesis (22/39), paresthesia (28/39), and facial palsy (23/39), and symptoms of dysautonomia also were observed during hospitalizations (3/39). The average time from vaccination to symptom onset was 11.3 days. A total of 34 case-patients received lumbar puncture; 30 had manifestations of albuminocytologic dissociation in the cerebrospinal fluid.

On the basis of the clinical diagnostic classification of GBS, we found that most case-patients had the classic form (22/39), followed by bilateral facial palsy with paresthesia (12/39), the paraparetic form (4/39), and GBS–Miller Fisher syndrome overlap variant (1/39). We defined all classic and paraparetic forms of GBS (26/26) as level 1 or 2 on the basis of the Brighton criteria (5). We identified the GBS subtype in 33/39 cases by electrophysiological examination; most reported case-patients had a diagnosis of acute inflammatory demyelinating polyneuropathy (23/33), followed by acute motor and sensory axonal neuropathy (4/33) and acute motor axonal neuropathy (3/33). For GBS management, 33 case-

patients received intravenous immunoglobulin and 2 received plasmapheresis. One case-patient died; 9 case-patients required mechanical ventilation during hospitalization. The scores on the GBS disability scale (5) were only available for 30 cases; 12 scored  $\geq 4$  (i.e., indicating bedridden or chair-bound status) during follow-up or after discharge.

Similar to previous reviews on GBS associated with COVID-19, we found that both COVID-19 and COVID-19 vaccination mostly cause the classic form of GBS (under the clinical diagnosis classification) and the acute inflammatory demyelinating polyneuropathy subtype (based on electrodiagnostic features) within 2 weeks of infection or vaccination (6–8). However, the bilateral facial palsy with paresthesia variant and initial onset symptoms of facial diplegia were more frequently found in GBS case-patients after COVID-19 vaccination.

Case series and reports can indicate safety issues and outline clinical features of diseases, but they cannot establish robust causal relationships between COVID-19 vaccination and GBS. Despite the benefits (e.g., increase in the number of persons not susceptible to infection and decrease in severe outcomes after infection) of COVID-19 vaccination far outweighing the potentially severe adverse events after infection (9), our findings highlight the need for vigilance in patients with neurologic symptoms after COVID-19 vaccination and for postvaccination surveillance programs to assess causality of GBS.

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## Limited Protection of Inactivated SARS-CoV-2 Vaccine against Wild-Type Strain and Variants of Concern

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In vitro determination of severe acute respiratory syndrome coronavirus 2 neutralizing antibodies induced in serum samples from recipients of the CoronaVac vaccine showed a short protection period against the original virus strain and limited protection against variants of concern. These data provide support for vaccine boosters, especially variants of concern circulate.

Circulation of novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants capable of evading vaccine-derived protection is challenging the efficacy of coronavirus disease (COVID-19) vaccines (1). The inactivated SARS-CoV-2 vaccine CoronaVac (Sinovac Biotech, <http://www.sinovac.com>), 1 of 2 COVID-19 vaccines licensed in Thailand, has been widely administered to health care workers. Clinical studies show CoronaVac efficacy against symptomatic COVID-19 ranging from 51% (Brazil) to 65.9% (Chile) and 100% against severe illness and illness requiring hospitalization (2,3). However, data on CoronaVac efficacy against variants of concern are very limited. Our study was approved by the Research Ethics Review Committee, Faculty of Medicine, Chulalongkorn University (Bangkok, Thailand) and recorded in the Thai Clinical Trial Registry (TCTR20210325003). Investigators adhered to U.S. Department of Defense AR 70–25 policies for protection of human subjects.

For this study, we enrolled 207 health care workers in Thailand who were fully vaccinated with 2 doses of CoronaVac (0.5 mL/dose, 2–4 wk between doses); all had received their first dose during February 22–March 12, 2021. Median age was 39 (interquartile range 30–51) years of age; 67 (49.6%) were men. Among study participants, 58 (28%) provided blood samples only at baseline (when the first dose was administered), 93 (44.0%) both at baseline and 2–3 weeks after the second dose, and 56 (27.0%) at baseline and at 2–3 weeks and 10–12 weeks after the second dose. Using an in vitro system (Appendix, <https://wwwnc.cdc.gov/EID/article/27/12/21-1772-App1.pdf>), we evaluated the ability of the serum of CoronaVac



# Guillain-Barré Syndrome Associated with COVID-19 Vaccination

## Appendix

**Appendix Table.** Clinical features of GBS associated with COVID-19 vaccination\*

Author name (country)	GBS rate	Age, y	Sex	Vaccine	Vaccination to symptom onset, d	Initial symptoms (dysautonomia)	Albuminocytologic dissociation (CSF protein, mg/dl)	Clinical classification	Electro- diagnosis	Brighton criteria†	Antiganglioside antibody	Treatment (drug dose)	Mechanical ventilation	Outcome (GBS disability scale‡)
Presented case (Taiwan)	1/18,801 (ChAdOx1 nCoV-19)	41	M	ChAdOx1 (1 <sup>st</sup> dose)	7	Paresthesia, facial diplegia (No)	Yes (159.8)	Bilateral facial palsy with paresthesia	Equivocal	NA	NA	IVIG (0.4g/kg/day for 5 days)	No	Survived (1)
Theuriet J, et al (France) (1)	NA	72	M	ChAdOx1 (1 <sup>st</sup> dose)	21	Myalgia, paresthesia, dysarthria, ascending paralysis, facial diplegia (No)	Yes (62.0)	Classic GBS	AIDP	1	Anti-GM3 IgM positive	IVIG (0.4g/kg/day for 5 days)	No	Survived (NA)
Hasan T, et al (UK) (2)	NA	62	F	ChAdOx1 (1 <sup>st</sup> dose)	8	Paresthesia, ascending paralysis (No)	Yes (90.0)	Classic GBS	AIDP	1	NA	IVIG (0.4g/kg/day for 5 days)	Yes	Survived (5)
Allen CM, et al (UK) (3)	4/712,050 (ChAdOx1 nCoV-19)	54	M	ChAdOx1 (1 <sup>st</sup> dose)	12	Paresthesia, facial diplegia (No)	Yes (162.6)	Bilateral facial palsy with paresthesia	Equivocal	NA	Negative	Prednisolone (60mg for 5 days)	No	Survived (NA)
		20	M	ChAdOx1 (1 <sup>st</sup> dose)	22	Paresthesia, facial diplegia (No)	Yes (123.2)	Bilateral facial palsy with paresthesia	Equivocal	NA	Negative	Prednisolone (60mg for 5 days)	No	Survived (NA)
		57	M	ChAdOx1 (1 <sup>st</sup> dose)	15	Back pain, paresthesia, dysarthria, facial diplegia (No)	Yes (247.1)	Bilateral facial palsy with paresthesia	Not done	NA	Negative	IVIG	No	Survived (NA)

Author name (country)	GBS rate	Age, y	Sex	Vaccine	Vaccination to symptom onset, d	Initial symptoms (dysautonomia)	Albuminocytologic dissociation (CSF protein, mg/dl)	Clinical classification	Electro- diagnosis	Brighton criteria†	Antiganglioside antibody	Treatment (drug dose)	Mechanical ventilation	Outcome (GBS disability scale‡)
		55	M	ChAdOx1 (1 <sup>st</sup> dose)	22	Paresthesia, facial diplegia no	Yes (89.0)	Bilateral facial palsy with paresthesia	Not done	NA	Negative	No treatment	No	Survived (NA)
Maramattom BV, et al (India) (4)	7/1,200,000 (ChAdOx1 nCoV-19)	43	F	ChAdOx1 (1 <sup>st</sup> dose)	10	Back pain, quadriparesis, facial diplegia (No)	Yes (85.0)	Classic GBS	AIDP	1	NA	IVIG	Yes	Survived (0)
		67	F	ChAdOx1 (1 <sup>st</sup> dose)	14	Paresthesia, quadriparesis, facial diplegia (No)	Yes (345.0)	Classic GBS	AMSAN	1	Negative	IVIG (NA) Plasmapheresis	Yes	Survived (4)
		53	F	ChAdOx1 (1 <sup>st</sup> dose)	12	Paresthesia, quadriparesis, facial diplegia (No)	Yes (120.0)	Classic GBS	AIDP	1	Negative	IVIG (NA)	Yes	Survived (4)
		68	F	ChAdOx1 (1 <sup>st</sup> dose)	14	Paresthesia, quadriparesis, dysphagia, facial diplegia (No)	Yes (75.0)	Classic GBS	AIDP	2	Negative	IVIG (NA)	Yes	Survived (4)
		70	M	ChAdOx1 (1 <sup>st</sup> dose)	11	Paresthesia, quadriparesis, facial diplegia (No)	NA	Classic GBS	AIDP	2	NA	IVIG (NA)	Yes	Survived (4)
		69	F	ChAdOx1 (1 <sup>st</sup> dose)	12	Paresthesia, quadriparesis, facial diplegia (No)	NA	Classic GBS	AIDP	2	NA	IVIG (NA) Plasmapheresis	No	Survived (4)
		69	F	ChAdOx1 (1 <sup>st</sup> dose)	13	Paresthesia, quadriparesis, facial diplegia (No)	Yes (83.0)	Classic GBS	AIDP	1	NA	IVIG (NA)	Yes	Survived (5)
Ogbebor O, et al (USA) (5)	NA	86	F	BNT162b2 (1 <sup>st</sup> dose)	1	Paraparesis (No)	Yes (162.0)	Paraparetic	Not done	2	NA	IVIG (NA)	No	Survived (3)
Patel SU, et al (UK) (6)	NA	37	M	ChAdOx1 (1 <sup>st</sup> dose)	14	Back pain, paresthesia, ascending paralysis (No)	Yes (177.0)	Classic GBS	Not done	2	NA	IVIG (2g/kg/day for 5 days)	No	Survived (NA)
Márquez Loza AM, et al (USA) (7)	NA	60	F	Ad26.COV2.S (1 <sup>st</sup> dose)	10	Back pain, paraparesis, facial diplegia (No)	Yes (140.0)	GBS / MFS overlap variants	AIDP	1	Negative	IVIG (2g/kg/day for 2 days)	No	Survived (NA)

Author name (country)	GBS rate	Age, y	Sex	Vaccine	Vaccination to symptom onset, d	Initial symptoms (dysautonomia)	Albuminocytologic dissociation (CSF protein, mg/dl)	Clinical classification	Electro- diagnosis	Brighton criteria†	Antiganglioside antibody	Treatment (drug dose)	Mechanical ventilation	Outcome (GBS disability scale‡)
Waheed S, et al (USA) (8)	NA	82	F	BNT162b2 (1 <sup>st</sup> dose)	14	Myalgia, paresthesia, paraparesis BP fluctuation	Yes (88.0)	Paraparetic	Not done	2	NA	IVIG (NA)	No	Survived (NA)
Razok A, et al (Qatar) (9)	NA	73	M	BNT162b2 (2 <sup>nd</sup> dose)	16	Paraparesis (No)	Yes (80.0)	Paraparetic	AIDP	1	NA	IVIG (0.4g/kg/day for 5 days)	No	Survived (0)
Nasuelli NA, et al (Italy) (10)	NA	59	M	ChAdOx1 (1 <sup>st</sup> dose)	10	Paresthesia, facial diplegia (No)	Yes (140)	Bilateral facial palsy with paresthesia	AIDP	NA	Negative	IVIG (0.4g/kg/day for 5 days)	No	Survived (NA)
Bonifacio GB, et al (UK) (11)	NA	66	M	ChAdOx1 (1 <sup>st</sup> dose)	7	Back pain, paresthesia, facial diplegia (No)	Yes (199)	Bilateral facial palsy with paresthesia	AIDP	NA	Negative	IVIG (NA)	No	Survived (1)
		43	M	ChAdOx1 (1 <sup>st</sup> dose)	11	Myalgia, paresthesia, facial diplegia Urinary retention	Yes (281)	Bilateral facial palsy with paresthesia	AIDP	NA	Negative	IVIG (NA)	No	Survived (2)
		51	M	ChAdOx1 (1 <sup>st</sup> dose)	7	Myalgia, paresthesia, facial diplegia (No)	Yes (514)	Bilateral facial palsy with paresthesia	AIDP	NA	Anti-GM3 positive, anti-GM4 borderline	No treatment	No	Survived (2)
		71	F	ChAdOx1 (1 <sup>st</sup> dose)	12	Back pain, Paresthesia, facial diplegia (No)	Yes (96)	Bilateral facial palsy with paresthesia	AIDP	NA	Negative	No treatment	No	Survived (2)
		53	M	ChAdOx1 (1 <sup>st</sup> dose)	8	Paresthesia, facial diplegia (No)	Yes (122)	Bilateral facial palsy with paresthesia	Not done	NA	Negative	No treatment	No	Survived (1)
McKean N, et al (Malta) (12)	NA	48	M	ChAdOx1 (1 <sup>st</sup> dose)	10	Back pain, facial diplegia, paresthesia, quadriparesis (No)	Yes (126.4)	Classic GBS	AIDP	1	Negative	IVIG (2g/kg/day for 5 days)	No	Survived (1)
James J, et al (India) (13)	NA	60	M	ChAdOx1 (1 <sup>st</sup> dose)	11	Quadriparesis, paresthesia, facial diplegia (No)	Yes (149)	Classic GBS	AMSAN	1	NA	IVIG (2g/kg/day for 5 days)	No	Survived (3)

Author name (country)	GBS rate	Age, y	Sex	Vaccine	Vaccination to symptom onset, d	Initial symptoms (dysautonomia)	Albuminocytologic dissociation (CSF protein, mg/dl)	Clinical classification	Electro- diagnosis	Brighton criteria†	Antiganglioside antibody	Treatment (drug dose)	Mechanical ventilation	Outcome (GBS disability scale‡)
		66	M	ChAdOx1 (1 <sup>st</sup> dose)	12	Ascending paralysis, paresthesia Urinary retention, BP fluctuation	Yes (84)	Classic GBS	AIDP	1	NA	IVIG (2g/kg/day for 5 days), Methylprednisolone (1000 mg for 3 days)	No	Survived (3)
		54	F	ChAdOx1 (1 <sup>st</sup> dose)	13	Quadriparesis, paresthesia, dysphagia (No)	NA	Classic GBS	AIDP	2	Negative	IVIG (2g/kg/day for 5 days), Methylprednisolone (1000 mg for 3 days)	No	Survived (2)
García- Grimshaw M, et al (Mexico) (14)	7/3,890,250 (BNT162b2)	33	M	BNT162b2 (1 <sup>st</sup> dose)	28	Facial diplegia (No)	Yes (67.1)	Bilateral facial palsy with paresthesia	AIDP	NA	NA	IVIG (NA)	No	Survived (1)
		25	M	BNT162b2 (1 <sup>st</sup> dose)	12	Paresthesia, quadriparesis (No)	Yes (64)	Classic GBS	AIDP	1	NA	IVIG (NA)	No	Survived (3)
		53	F	BNT162b2 (1 <sup>st</sup> dose)	6	Quadriparesis (No)	No (15)	Classic GBS	AMAN	2	NA	IVIG (NA)	Yes	Survived (5)
		72	M	BNT162b2 (1 <sup>st</sup> dose)	4	Quadriparesis (No)	NA	Classic GBS	AMAN	2	NA	IVIG (NA)	No	Survived (4)
		31	M	BNT162b2 (1 <sup>st</sup> dose)	11	Quadriparesis (No)	NA	Classic GBS	AIDP	2	NA	IVIG (NA)	No	Survived (3)
		67	F	BNT162b2 (1 <sup>st</sup> dose)	4	Quadriparesis (No)	No (30)	Classic GBS	AMAN	2	NA	IVIG (NA)	Yes	Expired (6)
		81	F	BNT162b2 (1 <sup>st</sup> dose)	3	Quadriparesis (No)	Yes (414)	Classic GBS	AIDP	1	NA	IVIG (NA)	No	Survived (4)
Trimboli M, et al (Italy) (15)	NA	25	F	BNT162b2 (2 <sup>nd</sup> dose)	5	Paraparesis, paresthesia (No)	No (NA)	Paraparetic	AIDP	2	NA	IVIG (0.4g/kg/day for 5 days)	No	Survived (2)
Tutar NK, et al (Turkey) (16)	NA	76	M	CoronaVac (2 <sup>nd</sup> dose)	5	Myalgia, ascending paralysis (No)	No (NA)	Classic GBS	AMSAN	2	Negative	IVIG (2g/kg/day for 5 days)	No	Survived (2)



Author name (country)	GBS rate	Age, y	Sex	Vaccine	Vaccination to symptom onset, d	Initial symptoms (dysautonomia)	Albuminocytologic dissociation (CSF protein, mg/dl)	Clinical classification	Electro- diagnosis	Brighton criteria†	Antiganglioside antibody	Treatment (drug dose)	Mechanical ventilation	Outcome (GBS disability scale‡)
Scendoni R, et al (Italy) (17)	NA	82	F	BNT162b2 (2 <sup>nd</sup> dose)	15	Ascending paralysis, paresthesia (No)	Yes (570)	Classic GBS	AMSAN	1	Anti-sulfatide IgG and IgM positive, anti- GM2 IgM positive, anti-GM4 IgM positive	IVIg (0.4g/kg/day for 5 days)	No	Survived (4)

\*AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy; BP, blood pressures; CSF, cerebral spinal fluid; GBS, Guillain-Barré Syndrome; IVIG, Intravenous immunoglobulin; MFS, Miller-Fisher Syndrome; NA, not available.

†The Brighton Criteria is a diagnostic tool for GBS, ranging from level 1 (highest level) to level 4 (lowest level) of diagnostic certainty by assessing the patient's clinical presentation, cerebrospinal fluid data and nerve conduction velocity findings.

‡GBS Disability Scale grades the patient's functional disability from 0 (healthy) to 6 (dead).

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